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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,470	07/21/2003	Debbi Drane	017227-0190	4517

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,470	DRANE ET AL.	
	Examiner	Art Unit	
	BAO LI	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,44,45,49-66 and 70-99* is/are pending in the application.

4a) Of the above claim(s) *56-62,77-83 and 86-99* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 44-45, 49-55, 63-66, 70-76, 84-85* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Summery

The amendment and response filed on Feb. 26, 2006 have been acknowledged. Claims 1 and 64 have been amended. Claims 2-43, 46-48, 67-69 were canceled. Claims 1, 44-45, 49-66, 70-99 are pending. Claims 56-62, 77-83 and 86-99 were withdrawn from consideration. Claims 1, 44-45, 49-55, 63-66, 70-76, 84-85 are considered before the examiner.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

2. Regarding the rejection of claims 1, 44, 49-55, 64-66, 70-76 under 35 U.S.C. 102(b) as being anticipated by Simmonds et al. (A) (WO 94/25602A1) or under 35 U.S.C. 102(e) as being anticipated by Simmonds et al. (B) (US Patent No. 6,881,821B2) or (C) (US 7,198,892B2) in light of the teaching by Sjolander et al. (Advanced Drug Delivery Reviews Volume 34, Issues 2-3, December 1998, Pages 321-338), the amendment and Applicants' argument have been respectfully considered, which are found persuasive to overcome the rejection. Because the factual argument points out all peptides taught by Simmonds et al. being

negatively charged, wherein the negatively charged antigen can not interact with the negatively charged carrier via electrostatic association.

3.

4. Claims 1, 44, 49, 50, 51, 54, 55, 64, 70-72, 75, 76 are still rejected under 35 U.S.C. 102(b) as being anticipated by Garcon et al. (WO 96/33739A1) in light of the disclosure by Hitomi et al. (Viral Immunology, 1995, Vol. 8, No. 2, pp. 109-119) and Barr et al. (Immunology and Cell Biology 1996, Vol. 74, pp. 8-25) for claim 85.

5. Applicants traverse the rejection and submit that 1). Garcon's reference only describes ISCOM once in the reference, 2). Saponin plus cholesterol do not always form ISCOM as examiner assumed in the previous office action, and 3). Garcon et al. do not teach or suggest selecting an antigen positively charged, and the complex comprising ISCOM and an HCV antigen being formed by an electrostatic interaction only.

6. Applicants' argument has been fully considered; however, it is not persuasive for the following reasons:

a. The claimed immunogenic complex is not limited to the product formed by electrostatic interaction only. Because the rejected claims use an open language "comprising" to describe the claimed immunogenic complex. It is known in the art that the immunogenic antigen adsorbed to the ISCOM complexes are formed by several mechanisms inherently possessed by the physical and chemical properties. For example, ISCOM is made by saponin and cholesterol, optionally with addition of phospholipids. They are matrix particles with hollow, spherical, cage like structures with around 40 nm in diameter and have negatively charged surfaces at a physiological pH (See review by Barr et al. Immunological and Cell Biology 1996, Vol. 74, pp. 8-25).Therefore, an antigen if it is suitable entrapped into the hollow, spherical cage structure of the ISCOM, it will inherently entrapped into regardless it is a negatively charged or positively charged.

b. It is also noted that the method for making ISCOM/antigen complex described in the prior art is same as the one described in the current Application. Therefore, an HCV antigen mixed together with ISCOM taught by prior art would be inherently same to the immunological complex cited in the current claims. Moreover, Carcon et al. do not limit

that HCV antigen as any particular one. The core antigen of HCV by nature is positively charged in light of the disclosure by Hitomi et al. (Viral Immunology 1995, Vol. 8, No. 2, pp. 109-119). Applicants' attention is directed to the case law of *In re Sussman*, 141 F. 2d 267, 60 U.S.P.Q. 538 (CCPA 1944), which cites "since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims." In the instant case, Applicant(s) is (are) claiming an invention employing the **same process steps** but the product(s) is (are) **alleged to be different**. If the claimed products are structurally different, Applicant is required to recite the missing steps to form the alleged different product(s) in view of the above cited decision.

c. Regarding the argument, the electronic interaction was not taught at the time when the present Application was filed, Applicants are directed to MPEP 2105, which cites: INHERENT FEATURE NEED NOT BE RECOGNIZED AT THE TIME OF THE INVENTION. There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. Schering Corp. v. Geneva Pharm. Inc., 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition by a person of ordinary skill in the art before the critical date and allowing expert testimony with respect to post-critical date clinical trials to show inherency); see also Toro Co. v. Deere & Co., 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004)("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention."); Abbott Labs v. Geneva Pharms., Inc., 182 F.3d 1315, 1319, 51 USPQ2d 1307, 1310 (Fed.Cir.1999) ("If a product that is offered for sale inherently possesses each of the limitations of the claims, then the invention is on sale, whether or not the parties to the transaction recognize that the product possesses the claimed characteristics."); Atlas Powder Co. v. Ireco, Inc., 190 F.3d 1342, 1348-49 (Fed. Cir. 1999) ("Because sufficient aeration' was inherent in the prior art, it is irrelevant that the prior art did not recognize the key aspect of [the] invention.... An inherent structure, composition, or function is not necessarily known.")>; SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1343-44, 74 USPQ2d 1398, 1406-07 (Fed. Cir. 2005) (holding that a prior art patent to an anhydrous form of a compound "inherently" anticipated the claimed hemihydrate form of the compound because practicing the process in the prior art to manufacture the anhydrous compound "inherently results in at least trace amounts of" the claimed hemihydrate even if the prior art did not discuss or recognize the hemihydrate).

d. MPEP also cites "[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." Atlas Powder Co. v. Ireco Inc., 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus, the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). Carcon et al teach an immunogenic complex with structurally and functionally same compounds/materials although the molecular interaction between the molecules that forms the complex is not explicitly or implicitly taught or may not be same, it does not make the structurally same product patentable different.

7. Regarding the limitation of properties of the immunogenic complex being able to induce a cytotoxic T lymphocyte response, since the complex is the ISCOM loaded by an antigen, it inherent exhibits same biological and immunological activity for stimulating the T cell activity as evidenced by Barr et al. (Immunology and Cell Biology 1996, Vol. 74, pp. 8-25). To this context, claim 85 is also inherently anticipated by the cited reference.

8. As it is discussed above, the disclosure of the cited reference still meet the limitation of the claims, the rejection is maintained.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The rejection of claims 1, 44, 49-55, 63-66, 70-76 and 84-85 under 35 U.S.C. 103(a) as being unpatentable over Simmonds et al. (A) (WO 94/25602A1) or (B) or (C) as cited above in view of the teaching by Cerny et al. (J. Clin. Invest. 1995 Feb; 95(2):521-30) has been removed in view of Applicants' amendment and persuasive argument.

11. The rejection of claims 1, 44-45, 49-55, 63-66, 70-76 and 84-85 under 35 U.S.C. 103(a) are still rejected as being unpatentable over Garcon et al. (WO 96/33739A1) as applied to claims 1, 44-55, 64-66, 70-76, and further in view of Cerny et al. (J. Clin. Invest. 1995 Feb; 95(2):521-30) for claims 63 and 84-85 has been withdrawn in view Applicants' persuasive argument, because the prior art do not teach which particular second positive antigen added to first positive antigen.

12. New ground rejection:

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 44-45, 49-55, 63-66, 70-76, 84-85 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for having an immunogenic composition comprising a negative charged organic carrier and a positive charged antigen, does not reasonably provide enablement for the claimed immunogenic complex formed by electrostatic interaction only. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

3. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988) are summarized below:

4. 1). Nature of the invention, 2). State of art, 3). Scope of the invention, 4). Unpredictability of the field, 5). Level of skill in the art, 6). Working example taught by

specification, 7). Guidance provided by the specification, 8). Amount of work to fulfill the scope of the claimed invention.

5. The nature of the invention is drawn to an immunogenic composition comprising a negative organic carrier of ISCOM made by mixing saponin and cholesterol, and an HCV antigen polypeptide overall being positive charged, wherein the complex is made by just mixing them together.

6. State of art teaches that immune-stimulatory complexes (ISCOMs) are stable complexes of cholestrol, phospholipid and Quil A (Saponin). They are nanoparticles in the size from 40-100 nm. They can be used as an antigen carriers as well as an adjuvant for producing both Th1 and Th2 types of immune responses. The nanoparticle by nature is negative charged organic carrier with a cage like structure. Therefore, they can be loaded or associated with antigens by various mechanisms, such as entrapping inside the cage structure or associated by a hydrophobic group, or a covenant or non-covalent bound or an ionic interaction by different charges between the antigen and the carrier. Incorporation of lipid or cholesterol molecules into the ISCOM increases the negative charge of the nanoparticles. Using ISCOM as a carrier to any polypeptide or peptide antigen can be made by just mixing the ISCOM with the antigen polypeptide or peptide as evidenced by Barr et al. (Immunology and Cell Biology 1996, Vol. 74, pp. 8-25) and Garcon et al. (WO 96/33739A1).

7. However, the state of art does not teach how to make an ISCOM/antigen complex via electrostatic interaction only. There is no such method available in the art to measure different associations between the hydrophobic or electronic interaction in the art and specification of current Application. Applicants in the specification does not teach how to prevent other mechanism from happening that an antigen is associated or loaded into the ISCOM nanoparticles, if the peptide or polypeptide antigen is in a size or hydrophobic status suitable for entrapped or hydrophobic associated with ISCOM. Therefore, it is unpredictable how such kind of antigen can be associated with ISCOM with electrostatic interaction only. There is no guidance in the specification for making and measuring the ISCOM/antigen complex by electrostatic interaction only.

8. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan

would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Double Patenting

9. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims 1, 44, 45, 49 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 6, 7, 8, 10 of copending Application No. 12,231,357. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the conflict claims are overlapping.

11. In the instant case, the rejected claims overlaps with the scopes of the reference claims for directing to an immunogenic composition comprising HCV fusion polypeptides all associated with ISCOM. Therefore, they are considered to be obvious each form other.

12. An obvious-type double patenting rejection is appropriate where the conflict claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887,225 USPQ 645 (fed. Cir. 1985).

13. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BAO LI whose telephone number is (571)272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nickol Gary can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Bao Qun Li/
Examiner, Art Unit 1648